RINDERPEST IMMUNITY
IN CALVES

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by

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CONTENTS

Since the selection of the caprinized, lapinized, avianized and avianized-lapinized strains of attenuated rinderpest virus, the problem of immunizing large numbers of cattle cheaply and effectively in Africa and Asia has been resolved. In recent years, the epizootiological picture has changed in countries where an efficient vaccination policy has been pursued. Today sporadic outbreaks are alleged to occur, usually in newly-weaned calves, inferring that any maternally-derived immunity has waned and the calves are susceptible to infection.

Calves, the progeny of immune dams, are regarded as poor subjects for active immunization against rinderpest. Furthermore, little is known of the immunological response of calves, the progeny of rinderpest susceptible dams.

This study was designed to clarify the problem by using standard serological techniques.

REVIEW OF THE LITERATURE

THE PRODUCTION OF ANTIBODIES BY YOUNG ANIMALS

The immunological responses of young animals to antigenic stimuli may differ from those of adults. Moll (1908) reported that one out of two young rabbits of about 3 weeks of age, previously inoculated several times with horse serum globulins, had a lower titre than an adult rabbit inoculated in the same way. Moll stated that sera of 3 weeks old rabbits inoculated with cholera vaccine had lower bacteriocidal titres than adult rabbits, and that production of agglutinating antibodies against _Vibrio_ _cholerae_ and of sheep cell haemolysins was less in young than in adult rabbits. Newborn guinea pigs were not sensitized so readily to sheep serum as adults, and produced less precipitins (Friedberger and Simmel, 1913). Similarly only 3 out of 30 infants produced agglutinins after vaccination with typhoid vaccine (Frankenstein, 1920). Halber, Hirszfeld and Mayzner (1927) found that after immunization against typhoid the agglutinating titre of the serum was lower in infants than in children aged 2-5 years. Happ (1920) reported that blood groups were seldom found in infants younger than one month and did not reach adult titre until 2 years old.

Freund (1930) compared the production of agglutinins against _Bacillus_ _typhosus_ and sheep cell haemolysin in young rabbits 1 or 2 days old, with that in adults. Only

2 out of 10 young rabbits produced B.typhosus agglutinins in detectable amounts whereas all the adults did so in higher amounts. All of 6 young rabbits produced haemolysin but in much smaller amounts than six adults. Production of precipitins against horse serum and egg white was much less in the young than in the adult rabbits. Arthus' phenomenon was not produced in young rabbits immunized with horse serum or egg white.

Baumgartner (1934a, b) investigated both quantitative and qualitative differences in anti-body production in rabbits of different ages. The responses of "young" (4-7 weeks old), "adult" (6-13 months old) and "aged" (two years old or more) rabbits to inoculations of sheep erythrocytes and killed B.enteritidis were determined. "Young" animals produced fewer antibodies than "adults" while "aged" animals were less able to produce antibodies than "adults". Qualitative differences in the sera from animals of different ages were also shown, the "avidity" being greater in "adults" than in young animals. Baumgartner (1937) further found that young rabbits (7-8 weeks old) produced less precipitins against horse serum than adult animals (2 years old), and that antisera produced in young rabbits tended to combine with specific antigen in different proportions to those of adults.

Published work on the immune response of young calves to antigenic stimuli is meagre. Henning (1953a, b) found that calves of less than 7 days old produced "H" but seldom "O" agglutinins following the inoculation of formalized aluminium hydroxide precipitated *Salmonella dublin* vaccine. Cattle receiving a similar vaccine (though 3 times as concentrated and in 4 times the dose), produced both "H" and "O" agglutinins. Kerr and Robertson (1954) reported that calves of less than 3 weeks old did not develop *Trichomonas foetus* agglutinins following one inoculation of antigen. Subsequent exposure revealed that the calves had acquired a tolerance to the antigen. The first unmistakeable response occurred when calves were at least 30 days old. Kerr (1956) found that only 1 of 6 calves of 7 days of age inoculated with living and dead *Brucella abortus* and *Salmonella dublin* antigens produced a detectable immunological response and then only to a low titre. Two of the calves inoculated possessed a passive immunity against *B.abortus*. Nevertheless, 1 day old calves reacted with an immunological response against skin homographs just as vigorously as adults (Billingham and Lampkin, 1957).

The first attempt to determine the time at which a species of animal became immunologically "adult" was that of Wolfe and Dilks (1948), who inoculated bovine serum into chicks aged from 1 day to 12 weeks and bled and tested their sera for precipitins 9 days later. Slightly less than 50 per cent of chicks injected on the first or third days after hatching gave detectable precipitins. A similar percentage of those inoculated at 1 week old produced antibodies, but the titres were considerably greater. The titres produced in 2 week old chickens increased and 19 out of 29 birds responded. At 3 weeks old, 15 out of 20 birds inoculated produced antibodies. At 4 weeks of age, 24 out of 31 responded. At 5 weeks of age, 30 out of 31 responded, and the titres were similar to those in chicks of 4 weeks of age. All chicks from 6-12 weeks of age gave detectable precipitins, the titres being higher. This seemed to indicate that at 5 weeks of age the precipitin response had almost reached its maximum. The authors considered that the results correlated well with the work reported by Herrick (1925), who studied the resistance of chicks to the nematode Ascaridia perspicillum. In chicks up to 15 days of age the parasite grew in the greatest amount, but in older chicks the parasite grew less and by 100 days of age resistance to the parasitic reached its maximum. However, Cannon and Longmire (1952) found that some chicks of a few days old accepted skin homographs, but they were always rejected by chicks of 2 weeks old.

Overman (1954a) suggested that the term "adult" per se has little meaning in biology, and that each individual is a mosaic of various ages which includes mental age, sexual age, etcetera. Overman investigated the antibody response of suckling mice to the inoculation of a killed mumps virus vaccine. He inoculated litters of various ages as well as adults. As the age increased, the ability to respond to the antigenic stimulus appeared and became more efficient. The critical period was between the ages of 7 and 14 days. None of the mice inoculated when less than a week old had detectable antibodies 3 weeks later. Nevertheless, all the mice except those inoculated when 1 day old were sensitized and gave a marked secondary response on re-inoculation. In further studies, Overman (1954b) showed that in suckling mice there was a correlation between the ability to form antibody and the resistance to mouse-adapted mumps virus.

Much attention has been focussed recently on the response of infants to diphtheria, pertussis and tetanus vaccines. Sako (1947) compared the agglutinin titres of children inoculated at various ages ranging from 2 weeks to 5 years, with 3 doses of an alum precipitated toxoid (A.P.T.) pertussis vaccine given at monthly intervals. Agglutinin titres were determined 2-4 months after the course of inoculation had been completed. Children below the age of 3 months as well as those of other age groups developed agglutinins. On the other hand, a similar study by

Peterson and Christie (1951a) revealed a trend for the response to be better in each succeeding older age group. Previously, di Sant'Agnese (1949a) had recorded consistently higher pertussis agglutinin titres in children inoculated at 6-12 months of age than in those inoculated at 7 days of age. In addition, children 6-12 months of age produced significantly higher diphtheria antitoxin titres then newborn infants. Tetanus antitoxin production in the two groups was similar, a finding also recorded by Peterson and Christie (1951b). However, Osborn, Dancis and Julia (1952a) reported that infants of 1 month or less did not respond as well as older infants following the single inoculation of a combined high titre tetanus and diphtheria toxoid, but that the production of tetanus antitoxin in infants of 1 month or under was more rapid than the production of diphtheria antitoxin. Vahlquist, Murray and Persson (1948) found that a single inoculation of diphtheria A.P.T. stimulated the production of diphtheria antitoxin in babies a few days old, but the response was slower than in those of 2-3 or 6-8 months of age. Three months after inoculation, the titres in babies of all groups were similar. Osborn _et al_. (1952a) also found that children of 1 month or less at the time of inoculation of a diphtheria A.P.T. did not respond as quickly as older infants; in addition the titres in the younger infants did not reach levels achieved by the older infants. Infants under 2 weeks old responded much less than those 1 month old, who in turn had a much smaller response than infants 2 months old.

Thus a general agreement emerges that infants a few days old can respond to some antigens with the production of antibodies. Findings on the rate of production of antibodies and the titres attained have varied. As Sako (1947) and Vahlquist _et al_. (1948) pointed out, the previous poor results in newborn infants were probably due to inferior fluid toxoids, to the failure to recognise the inhibiting effect of maternally-derived antibodies, and to ignorance of the slow response of babies. Vahlquist _et al_. suggested a further error caused by comparing the response of infants with that of adults, many of whom had probably been actively immunized earlier in life and thus were showing secondary, not primary, antitoxin responses.

The modern concept is that very young animals can produce antibodies. Variations are explained by differences in antigen and in techniques used to measure the responses.

MATERNALLY-DERIVED ANTIBODIES

The defence machanism of the young mammal against infections diseases differs from that of the adult. Mammalian mothers possessing an active immunity against certain diseases confer upon their progeny a passive immunity, which may last until the young animal produces an active immunity. Bollinger's (1877) was the first report of this phenomenon; he found that lambs born of recently vaccinated ewes were immune to cowpox. Confirmation quickly followed. Chauveau (1880) immunized Algerian sheep against anthrax during pregnancy and demonstrated that the offspring were also immune.

Ehrlich (1892) in his classical experiments showed that the newborn animal may obtain maternally-derived immunity via the placenta and the mammary gland. Further evidence of the transmission of passive immunity via the mammary gland was given by Famulener (1912) who concluded that the transplacental route was of little importance in the transfer of passive immunity from the goat to the kid. In humans, colostrum was a negligible factor in the transfer of passive immunity (Kuttner and Ratner, 1923).

Pioneer work on the value of colostrum to the newborn calf was carried out by Theobald Smith and his co-workers in their investigations into the death of newborn calves from <u>Bacterium coli</u> infections. If deprived of colostrum 75 per cent of newborn calves died from B.coli septicaemia. If given colostrum they survived (Smith and Little, 1922a). Similarly, calves born of immune dams did not possess Brucella abortus agglutinins at birth, but these antibodies appeared in the serum soon after ingesting colostrum, and the calves' serum titres were similar to or greater than those of the dams (Little and Orcutt, 1922). Furthermore, the colostrum was replaceable by the immune serum (Smith and Little, 1922b). Howe (1924) showed that the blood of newborn calves lacked pseudoglobulin and euglobulin, but these appeared quickly following the ingestion of colostrum.

Most workers agree that calves at birth lack antibodies. Brucella abortus agglutinating antibodies (Little and Orcutt, 1922; McAlpine and Rettger, 1925; McDiarmid, 1946), diphtheria antitoxin (Mason, Dalling and Gordon, 1930), Trichomonas foetus agglutinating antibodies (Kerr and Robertson, 1946) and Rickettsia burneti complement-fixing antibodies (Winn and Elson, 1952) were absent from the sera of calves born of dams possessing these antibodies until after the ingestion of immune colostra. The findings of Winn and Elson (1952) were unusual in that when colostrum containing R.burneti antibodies was fed to newborn calves, the antibodies appeared in the sera of those born of serologically positive, but not those of serologically negative dams. However, this extraordinary finding requires confirmation.

Hansen and Phillips (1947) showed that absorption of gamma globulin occurred during the first 24 hours of the calf's life. Comline, Roberts and Titchen (1951) artificially introduced immune colostral whey into the small intestines of calves aged 6-27 hours and recovered <u>Br. abortus</u> agglutinins in the lymph of the thoracic ducts. When whey was introduced into calves aged 63-65 hours, the agglutinins were demonstrated in low titres or were absent. Campbell, Sarwar and Petersen (1957) claimed "effective absorption of antibody from the gastrointestinal track does occur after the neonatal period; thus transmission of immunity with milk may be presumed to occur for the duration of nursing". Campbell <u>et al</u>. gave no experimental data to support this hypothesis but quoted the work of Gruskay and Cooke (1955) which suggested that in babies the absorption of unaltered protein was facilitated in infantile diarrhoea.

Little is known of the relationship of antibodies in the serum and the colostrum. Henning (1953a) reported that in cows immunized with a <u>Salmonella dublin</u> vaccine the titre of "H" agglutinins in the colostrum varied from 2-32 times that of the serum, whereas the titre of "O" agglutinins in the colostrum was rarely more than twice that of the serum. In 8 immune ewes the ratios

The latter author concluded that the duration of Br.abortus agglutinins in calves born of immune dams was from 1-18 weeks. Further, both the titre in the calf after suckling and the period of persistence depended upon the titre of the colostrum. A similar relationship between the initial titre in the young animal and the duration of immunity was found by Alexander and Mason (1941) who investigated the transmission and persistence of horse sickness antibodies from immune mares to their foals. The serum titre of 1/64 in one foal 16-30 hours after birth dropped to 1/4 at 75 days and was zero at 125 days after birth, whereas in another foal the initial titre was 1/512 at 1/4 at 175 days and zero at 325 days of age. Bruner, Edwards and Doll (1948) found that 5 foals from mares which had been immunized with a Salmonella abortusequi vaccine lost their maternally-derived agglutinins between 1 and 6 months of age. Recently Schneider (1955) reported that in calves born of highly immunized dams, maternally-derived foot and mouth disease antibodies persisted for about 8 weeks after birth. Ott (1956) without giving any experimental evidence, postulated that in the pups of bitches immune to distemper, "when the puppy reaches six weeks of age, the antibody titre is extremely low; although this low level may persist for a variable period". Gillespie (1956) reported that maternally-derived distemper neutralizing antibodies were demonstrable in pups for from 5 to 12 weeks after birth. Karzon (1955) found that in babies a maternally-derived distemper or related antibody persisted for periods up to 6 months after birth.

Estimates of the half-life of passively acquired antibodies have been made. In human infants the half-life of maternally-derived diphtheria antitoxin was 4½ weeks (Barr, Glenny and Randall, 1949). In lambs the half life of maternally-derived diphtheria antitoxin was 28 days (Barr, Glenny and Howie, 1953). Placenta-passing rhesus antibodies had a half-life of 30 days provided an allowance was made for the dilution factor due to the increase in body weight with age when calculating the result (Wiener, 1951).

Wiener applied his formula to already published data (Neill _et al._, 1932; Barr _et al._, 1949; Mason _et al._, 1930) and found that the half-lifes of the antibodies concerned were always about 30 days. He, therefore, suggested that the period of 30 days applied to all sera gamma globulins. However Dixon, Talmage, Maurer and Deichmiller (1952) found that the half-life period varied widely from species to species and they suggested that the half-life of gamma globulin depended in part upon the metabolic rate of the host. Furthermore, they found that age affected the half-life. Homologous gamma globulins labelled with I^{131} were used and it was found that in children aged between 6 months and 8 years the half-life was 20.3 days compared with 13.1 days in adults. These results agreed well with the half-lifes of homologous antibodies. The average half-lifes of Brucella abortus and Trichomonas foetus agglutinins were 14-20 days in calves receiving immune colostrum (Kerr and Robertson, 1954). However, the range was wide and in one calf the half-life of Tr. foetus antibody was 57 days.

ACTIVE IMMUNIZATION OF ANIMALS POSSESSING MATERNALLY-DERIVED ANTIBODIES

The presence of maternally-derived antibodies in young animals may interfere with the development of an active immunity. With the exception of diphtheria immunity in infants and rinderpest immunity in calves published work on the subject is meagre.

Park, Zingher and Serota (1914) considered that diphtheria toxin-antitoxin injections were inadvisable for infants less than 6 months old because most still retained passive antitoxic immunity from their mothers. Similarly Greengard and Bernstein (1935) considered that maternally-derived diphtheria antitoxin interfered with the active production of antitoxin. In recent years the problem of actively immunizing infants possessing passive diphtheria immunity has received much attention and most workers found that maternally-derived diphtheria antitoxin did not necessarily prevent the development of an active immunity (Cooke, 1948; Vahlquist, Murray and Persson, 1948; Vahlquist, 1949; di Sant'Agnese, 1949b, Barr, Glenny and Randall, 1949; Greenberg and Fleming, 1950, 1951; Christie and Peterson, 1951; Osborn, Dancis and Julia, 1952b). Estimates of the highest level of maternally-derived antitoxin which allowed the development of an active immunity by all inoculated babies varied from 0.02 (Vahlquist et al,1948; Vahlquist, 1949) and 0.04 units per ml. (Barr et al., 1949) to 0.1 units per ml. (Christie and Peterson, 1951; Osborn et al., 1952b). Levels of passive immunity which always prevented active production of antitoxin varied from 0.1 (Vahlquist et al., 1948; Vahlquist, 1949; Barr et al., 1949) to 1.0 unit per ml. (Christie and Peterson, 1951). Osborn et al. (1952b) suggested that the use of more potent antigen may have accounted for the higher critical level which they found compared with that reported by Vahlquist (1949). di Sant'Agnese (1949b), Vahlquist et al. (1948) and Greenberg and Fleming (1950, 1951) reported that infants possessing maternally-derived diphtheria antitoxin produced antibodies slower than infants which lacked antitoxin before inoculation; however the latter workers found that 1 year after inoculation there was no significant difference between the average titres of the two groups. In some infants although the maternally-derived antitoxin inhibited the active production of antibodies, the antibody-forming mechanisms were sensitized as shown by typical secondary responses on re-inoculation with diphtheria toxoid later (Osborn, Dancis and Julia, 1952b.)

Similarly critical levels were found in lambs by Barr, Glenny and Howie (1953), who invetigated the immunological response of lambs from immunized ewes to diphtheria toxoid. They found that those lambs which, at the time of the first injection possessed a total antitoxin content which neutralized 40% or less of the injected toxoid actively produced antitoxin but not when the passive antitoxin was greater than 40%. Good secondary responses were given by all lambs whose antitoxin content at the time of the first injection was twice that which would be sufficient to neutralize all the antigen injected, but where the total antitoxin content of the lamb was between 2.5 and 6 times the binding power of the injected antigen the secondary response was poor. Some lambs with a still greater passive immunity gave no active response to the second injection of toxoid.

Henning (1953a) was unable to actively immunize calves aged 1-14 days, the progeny of immune dams, with a <u>Salmonella dublin</u> vaccine. He considered that such calves aged less than two months would not actively produce antibodies. Alexander and Mason (1941) found that 4 foals, aged between 76 and 190 days, the progeny of mares immunized against African horse sickness, did not produce an active immunity following the inoculation of an attenuated horse sickness virus.

Ott (1956) stated that 6 week old pups, the progeny of bitches which have an "average" or "low" grade of immunity to distemper, would respond to the inoculation of an egg-adapted attenuated distemper vaccine with the active production of antibody, whereas pups of the same age from mothers with a "high" level of antibody would not produce antibody. Ott gave no experimental data. He further stated that there "has been no indication that the passively transmitted maternal antibodies have persisted in high enough concentration to interfere with vaccination of any puppy eight weeks of age or older".

RINDERPEST IMMUNITY IN CALVES

As early as 1915, Montgomery in Kenya reported that the rinderpest immunization of calves under 6 months of age was not always satisfactory. Many later workers considered that these difficulties were associated with the progeny of immune dams (Croveri, 1919; Askar, 1924; Doutressoulle, 1924; Rabagliati, 1924; Walker, 1929, 1930; Jacotot, 1932; Hall, 1933; D'Costa and Balwant Singh, 1933; Banerji, 1933). A contrary view, that young calves from immune dams may be satisfactorily immunized, was expressed by Edwards (1927) who reported that very young calves were immunized by the serum-simultaneous method. The calves seldom exhibited a thermal reaction following inoculation. The immunity was said to be a solid one for 2 years following vaccination. Edwards did not state whether the dams were immune or not, but they appear to have been so from the paper of D'Costa and Balwant Singh (1933) who continued rinderpest calfhood immunity experiments in the same herd, and stated that the cattle were immune.

Croveri (1919) working in Somaliland, after experiments in which 9 calves from immune dams were inoculated by the serum-simultaneous method, concluded that the milk of an immune dam gave to and maintained in the calf by means of suckling, a state of passive immunity which lasted until weaning at 3 months of age. Thereafter the immunity declined. Croveri considered that between the time during which the calf was certainly immune, during suckling and for some time afterwards, and the time when it would show a characteristic clinical reaction following serum-simultaneous vaccination, a period occurred during which the calf could be immunised, but the presence of small amounts of antibodies reduced the clinical reaction to vaccination. His statement that calves derived a passive rinderpest immunity from their immune dams through the milk was based on a calf, delivered by Caesarean section, which did not receive its dam's colostrum and which reacted to serum-simultaneous vaccination when 11 weeks of age. Another calf of the same age, born of an immune dam, which had been suckled normally did not react. However, the evidence is not conclusive as some workers (Askar, 1924; D'Costa and Balwant Singh, 1933) have claimed that calves from immune dams and less than 2 months of age may react to serum-simultaneous inoculation. Most authors have assumed that the passive immunity of calves born of rinderpest immune dams was obtained via the colostrum, though

Rabagliati (1924) considered that calves were born with a high antibody content of their tissues, but gave no details of experimental evidence. Gillain (1944) put forward the view that calves were immune at birth, as two calves, said to have been separated from their dams at birth and fed on milk from rinderpest susceptible cows, did not show any thermal reaction following the inoculation of caprinized rinderpest virus when aged 5 and 10 weeks respectively. Hale, Walker, Maurer, Baker and Jenkins (1946) considered "no immunity is conferred to calves born of vaccinated animals". This conclusion was reached after 2 pregnant cows were immunized with avianised rinderpest vaccine 8 and 16 days respectively before calving. Both cows were later found to be immune on challenge. However, no rinderpest neutralising antibodies were detected in the colostrum of the cows or in the sera of calves at any time after birth, and both calves were susceptible to challenge with bovine rinderpest virus 67 and 62 days respectively after birth.

Attempts to immunize young calves born of rinderpest immune dams by various vaccines or by challenge with bovine rinderpest virus, have given some information on the duration of the maternally-derived immunity, and of the value of attempting to immunize animals possessing such passive immunity. A difficulty associated with interpreting results obtained from calves inoculated with rinderpest virus and immune serum (the serum-simultaneous method of vaccination) is that the serum used may have contained sufficient rinderpest antibody to suppress the normal thermal reaction, and that this suppression may have been attributed to the possession of a maternally-derived immunity. Askar (1924) found that in one series of 34 calves born of immune dams and less than 5 months of age which had been inoculated by the serum-simultaneous method, none gave a positive thermal reaction, 24 were negative and 10 doubtful. In another series of 29 calves from immune dams and under 5 months old, 12 were positive, 12 doubtful and 5 negative, all the negative calves being less than 2 months old. Askar concluded that calves born of rinderpest immune mothers were susceptible to the disease after being weaned at 4 months of age. D'Costa and Balwant Singh (1933) inoculated groups of calves of various ages from immune dams by the serum-simultaneous method and challenged them with bovine virus 3-48 months later. Twenty-eight of 37 calves aged up to 5 months, 33 of 36 of 6-8 months, and 23 of 25 aged 9-24 months at the time of the serum-simultaneous inoculation were considered to have been successfully immunized. The authors concluded that the inoculation of calves under 4 months of age was of little practical value, whereas the inoculation of older calves was economical, but that the best results could be obtained by further inoculation of virus by itself 12-18 months after the serum-simultaneous inoculation. Similar results were obtained by Banerji (1933) who attempted to immunize calves from immune dams by a serum-simultaneous inoculation in which the virus was a caprinized strain. On challenge 12-31 months later, 5 out of 5 calves innoculated when less than 3 months of age were susceptible. In addition, 1 out of 3 and 1 out of 6 calves inoculated when aged 4-6 months and 7-11 months respectively were likewise susceptible.

Several workers including Rabagliati (1924) have inoculated young calves from immune dams with bovine rinderpest virus alone. He found that 1 of 7 calves aged 1 month and 1 of 3 calves aged 5 months reacted. A calf from an immune mother challenged with bovine rinderpest virus at 5 months of age did not react. When challenged 14 months later the calf still did not react. In other words, calves could be immunized without the production of a thermal reaction. Carmichael (1934), inoculated bovine rinderpest virus into 5 calves from immune dams and found that 2 calves aged 32 and 64 days respectively showed distinct thermal reactions but recovered, another calf aged 2 days showed a very mild reaction whereas 2 calves aged 7 and 8 days respectively had marked clinical reactions and died and typical rinderpest lesions were found on post mortem examination.

Rabagliati (1924) also showed that young calves, born of immune dams immunized by the serum-simultaneous method before or during pregnancy, possessed some immunity against rinderpest, but he considered that this resistance was not so great in calves from dams immunized before than in calves from dams immunized during pregnancy. Calves aged 12-18 months, from immune dams, were satisfactory subjects for immunization by the serum-simultaneous method. Walker (1921) found that only 6 of 15 calves aged less than 5 months from immune dams reacted to challenge whereas 6 of 7 unweaned calves (age of weaning not stated) from susceptible dams reacted to challenge and died. Jacotot (1932) found that 1 of 4 three-month-old calves, all of 3 six-month-old calves, both of 2 nine-month-old calves, and all of 47 one-year-old calves from immune dams reacted to challenge with bovine rinderpest virus. The same author gave an example of the value against natural rinderpest infection of the passive rinderpest immunity of calves born of immune dams. An outbreak of the disease occurred among a group of calves, all of which were exposed for several days. Four of 114 calves (3.5%) of less than 3 months, 18 of

120 (15%) of 3-6 months and 39 of 85 (45.8%) of 6-9 months of age contracted the disease. Jacotot also inoculated calves 1, 3, 5, 7, 9 and 11 months old all from immune dams, by the serum-simultaneous method and challenged them 12-15 months later. He found that the calves aged up to 9 months at the time of the serum-simultaneous inoculation reacted to challenge. He concluded that virulent rinderpest virus was generally without effect in calves from immune parents up to the age of 3 months, but that the passive immunity waned between 3-6 months of age, that serum-simultaneous inoculation did not give a solid immunity in calves aged less than 10 months, and that in calves of 3 months of age or less hardly any immunity at all was produced.

Doutressoulle (1924) found that the serum-simultaneous inoculation of a 6-month-old calf from an immune dam did not immunize the animal as it was susceptible to challenge 10 months later. Five calves from immune dams, challenged with bovine rinderpest vinus, showed oscillating temperqtures and were immune to a second challenge 3 months later; 5 calves aged 1 year from immune dams reacted severely to challenge. Another 13 calves aged 1-6 months from immune dams were inoculated with bovine rinderpest virus and did not react. On a second challenge later 6 out of 8 calves reacted. Gillain (1944) inoculated caprinized rinderpest virus into calves from immune dams. Only 1 out of 19 calves aged 1-6½ months reacted, whereas 12 of 14 aged 7-19 months reacted, the two exceptions being aged 14 and 15 months respectively. Gillain (1945) quoted Daubney's view that the resistance of young calves to rinderpest vaccine inoculation might be due as much or more to an age factor than to immunity transmitted by the milk of the immune dam. Gillain therefore inoculated calves from immune and non-immune dams with caprinized rinderpest virus. All of 17 calves from non-immune dams reacted, whereas of 8 calves from immune dams 7 did not react and 1 was doubtful. The author concluded that the resistance was not due to an age factor. Milne (1956) inoculated groups of calves of various ages, born of immune dams, with caprinized rinderpest virus noted the thermal reactions, challenged the animals for a second time later with the same virus and again noted the thermal reactions. He concluded that the passive immunity may last as long as 13-19 months after birth, that the inoculation of calves of 6-12 months of age from immune dams was of doubtful value, that the inoculation of calves of 2-6 months of age from immune mothers was of little use and that some calves which react to caprinized rinderpest virus when 2-6 months old do not necessarily retain an immunity, as one calf of this age which reacted to the first KAG inoculation also reacted again to a second inoculation 7 months later. Marqué and Koumaré Falley (1949, 1950) considered that inoculation with caprinized rinderpest virus produced an immunity in calves which lasted until the animals were weaned. They considered that it partially or completely disappeared after weaning, because 12 calves, each of which had been inoculated with caprinized rinderpest virus when young, reacted to challenge with bovine virus at the point of weaning. It was not stated if the calves were from immune dams, or what the age of weaning was. Calves immunized with caprinized virus at the time of weaning were immune to challenge 15 days later and to rechallenge 15 months later. The authors suggested that unweaned calves should be inoculated and re-inoculated at weaning time.

After inoculating calves of various ages from immune dams with bovine rinderpest virus, Jacotot and Colson (1935) concluded that the passive immunity was present in calves at 7½ months of age but not at 11½ months.

Hall (1933) considered that the passive rinderpest immunity obtained from the immune dam lasted until weaning, after which it waned and eventually disappeared. Within 6 months of weaning little or no resistance to infection remained. Daubney (1934) stated that calves outgrew within a few months the immunity conferred by 2 or 3 doses of inactivated vaccine, the younger the animal was at the time of vaccination the more rapidly the immunity was lost. The immune status of the dams was not given. Poole (1921) advised that calves of less than 9 months old should not be inoculated by the serum-simultaneous method. Brandt (1921), considered that it was likely that calves born of rinderpest immune cows possessed a passive immunity which was later lost. He reported that some calves of less than 6 months of age reacted after inoculation by the serum-simultaneous method but at a later period had contracted rinderpest. He did not give the immune status of the dams. Recently Robson (1956) reported that an adjuvant type inactivated rinderpest vaccine had no effect on calves aged 2 months or less from immune dams, but immunized 60% of calves inoculated when 2-6 months old compared with 34% of calves of the same age group inoculated with caprinized rinderpest virus.

Tarantino (1928) quoted the opinion of the inhabitants of Eritrea that calves born of immune dams were immune until weaning at 5-6 months of age.

The published work on passive rinderpest immunity in calves and the problem of immunizing such calves suggests that:

1. Calves born of rinderpest immune dams possess a passive immunity which is probably acquired via the colostrum. This conclusion is based on analogy with other work but is not proven with rinderpest.

2. The duration of this immunity varies considerably. Estimates range from a few days to 19 months.

3. This passive immunity may interfere with the production of an active immunity, especially in calves under 3-6 months of age.

Because of the wide divergences of opinion on the problem of active and passive rinderpest immunity in calves, a re-assessment based on the use of a neutralization test for rinderpest antibodies was made to find solutions to the following problems:-

(a) What is the immunological response of young calves from rinderpest susceptible dams to lapinized rinderpest vaccine?

(b) What is the mode of transfer of rinderpest antibodies from the immune cow to her calf and how long do such antibodies persist in the calf?

(c) Can calves of more than a few days old, consuming milk containing rinderpest antibodies absorb these antibodies from their intestinal tracts?

(d) What is the immunological response of calves aged from a few days to 12 months from immune dams, to caprinized rinderpest vaccine?

We hoped that answers to these questions would help to clarify the problem of immunizing young calves born of rinderpest immune dams.

MATERIALS

Cattle: In the rinderpest immunization of calves, animals of several breeds were used. Those that were the progeny of immune dams were East African Shorthorn-Zebus and were weaned at 9 months of age. Calves aged from 1 day to 2 months, the progeny of susceptible dams were either Ayrshire, Friesian or crossbred European-Zebu. Rinderpest susceptible cattle aged 2 years were crossbred European-Zebus. The 2 dams used to determine the effect of feeding milk from rinderpest-immune dams to calves, were of the Friesian breed. All the other immune dams were vaccinated 6-17 months before parturition with lapinised rinderpest virus followed 2-4 weeks later with caprinized rinderpest virus (K.A.G.) All were reared and kept on rinderpest-free farms. Both East African Shorthorn-Zebu and crossbred European-Zebu calves, the progeny of rinderpest immune dams, were used to determine the mode of transmission of maternal antibodies and their half-life in the calf. The history of these calves and the immunological status of the dams is given in Table 1.

TABLE 1

History of Calves Used for Determining the Duration of Passive Immunity.

Calf Number and Management	Dam Number, Time and Method of Rinderpest Immunization.
1592 Cross-bred European Zebu. Weaned at 6 months of age.	1131 Immunized with K.A.G. followed 3 weeks later by challenge with bovine rinderpest virus 5 months before parturition.
1722 Cross-bred European Zebu. Weaned at 6 months of age.	199 Immunized with K.A.G. 10 months before parturition.
420)East African Shorthorn 421)Zebus. All weaned at 422)9 months of age. 425) 433)	221)Immunized with lapinised 212)rinderpest vaccine, 240)followed 2-4 weeks later 219)with K.A.G. vaccine 213)15 months before parturition.

RABBITS: The rabbits were of the Albino, Chinchilla, Belgian Hare and Rex breeds and their crosses, aged 3½-6 months. All were equally susceptible to lapinised rinderpest virus.

RINDERPEST VIRUS STRAINS.

Lapinised Rinderpest Virus: The Nakamura III strain of lapinised rinderpest virus of the 16th and 19th Kabete passages respectively was used for the vaccination of calves and adult~~s~~ controls born of rinderpest susceptible dams. Virus of the 18th Kabete passage used for other cattle inoculations. On arrival at Kabete from China in 1949, the virus strain had undergone 795 serial rabbit passages. Virus used in neutralization tests was of the 15th, 17th and 18th Kabete passages. Aliquots of virus were stored in ampoules at minus 25°C. as a freeze-dried vacuum sealed 25 per cent. infected rabbit tissue suspension (Brotherston, 1951).

Caprinized Rinderpest Virus: The Kabete-Vom-Kabete strain of caprinized rinderpest virus at the 619th passage level, was used. Aliquots of the virus were stored at minus 25°C. as vacuum-sealed ampoules of freeze-dried infected goat spleen.

METHODS

Management of Cattle: In the immunization of calves, the progeny of rinderpest susceptible dams, with lapinised rinderpest virus, calves aged from 1-68 days, and 5 adult cattle aged 2 years, were each inoculated subcutaneously with 80 cattle ID_{50} of lapinised rinderpest virus. The virus was in the form of a freeze-dried infected rabbit tissue suspension reconstituted with normal saline and injected in 2ml. doses.

The calves, the progeny of rinderpest immune dams, used for determining the mode of transmission of maternal rinderpest antibodies, and their half-life in the calf, were separated from their dams immediately after birth and bled before being allowed to suckle, with the exception of calf 1592 which was born unobserved. At the same time, blood and colostrum samples were obtained from the dams. The calves were allowed to suckle, then were bled 30-48 hours later and at 30 day intervals after birth for periods up to one year. Samples of some of the dams' milk were obtained during the period up to 2 weeks after parturition. In the experiment to determine whether calves of more than 2 days old could absorb rinderpest antibodies from their intestinal tracts colostrum samples were obtained 2-3 hours after calving from 2 rinderpest-susceptible cows.

One day after calving the 2 cows and their calves were bled and the cows inoculated subcutaneously with 80 cattle ID_{50} of lapinised rinderpest virus. The cows and their calves were bled 7, 14, 21 and 42 days later. Milk samples were obtained from the 2 cows at intervals during the period up to 21 days and again 42 days following lapinised rinderpest virus inoculation. Each calf was given daily 1 gallon of its dam's milk for 6 weeks after birth.

In the attempts to immunise calves, the progeny of rinderpest-immune dams, with caprinised rinderpest virus, 65 animals were allocated on the basis of age to 13 groups of ages 1-6 days, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 and 12 months. The calves were bled and each inoculated subcutaneously with 2ml. of freeze-dried K.A.G. infected goat spleen that had been reconstituted with normal saline to give 100 cattle ID_{50s} of caprinised rinderpest virus per ml. The morning rectal temperatures of the calves were recorded for 2-3 weeks after K.A.G. virus inoculation. All calves in which a temperature rise of $2^{o}F.$ above the normal occurred for 3 days during the period 3-8 days following the inoculation of K.A.G. virus were considered to have shown a thermal reaction. The calves which also showed signs of diarrhoea were noted. The calves were bled 21 days and 1 year (365 days) after inoculation. All the dams whose calves possessed no rinderpest antibodies in their sera before K.A.G. inoculation were bled approximately 23-24 months after immunization and screened for neutralising antibodies. Six of the calves from immune dams which were inoculated with K.A.G. virus when aged 3 days to 7 months but were not actively immunized as a result as shown by the absence of serum antibodies 1 year later were bled, re-inoculated with 80 cattle ID_{50} of lapinized rinderpest virus 12-15 months after the K.A.G. inoculation, and bled 4 and 21 days later

Sera and wheys were titrated for rinderpest neutralising antibodies.

Sera: Cattle were bled from the jugular vein into sterile 1 ounce bottles, or 2 ounce tubes. The blood samples were allowed to clot and after standing overnight on the bench at a temperature of approximately 16-22°C., the sera were removed, centrifuged and stored in screw-capped bottles at minus 25°C for periods up to 15 months.

Colostrum and Milk Wheys: Approximately 200 ml. of colostrum or milk was warmed to 37°C and about

0.1g. of rennet powder* added. Colostrum and milk samples were allowed to stand on the bench overnight to clot, and the whey removed, centrifuged and stored in screw-capped bottles at minus 25°C for periods up to 15 months.

Tests for Rinderpest Neutralizing Antibodies.

Sera and wheys were inactivated by incubation in a 56°C waterbath for 30 minutes before dilution. Normally 5-fold dilutions of the serum or whey under test were prepared using "Lemco"** broth of pH 7.2-7.4 as a diluent. In each test 3 or 4 dilutions were used. The contents of 6 ampoules of freeze-dried lapinised rinderpest virus were reconstituted to original volume with sterile distilled water, and this diluted to 1:10 with "Lemco" broth and centrifuged for 3 minutes at 1500 r.p.m. to remove large particles of tissue. The supernatent was removed and further diluted with broth, so that each ml. would contain approximately 200 rabbit ID_{50s} per ml. if incubated for one hour in a37°C water bath. Equal volumes of the virus and serum dilutions were mixed and incubated

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* "Ha-La" Brand. Manufactured by Chr. Hansens Laboratory Ltd., Reading, England.

** Prepared from "Lab-Lemco" manufactured by Oxo Ltd., London, England.

in a 37°C. waterbath for one hour. The serum-virus mixtures were inoculated intravenously into rabbits in 1 ml. doses, 5 animals being used per dilution. Between the time of incubation and inoculation the bottles of serum-virus mixtures were kept on ice, in the shade. The controls included in each test were a virus titration, a known non-immune serum-virus mixture and the titration of a standard immune serum. The virus titration was to check the viability and to give the number of rabbit ID_{50s} in each ml. of the serum-virus mixtures, and the negative serum was a check of the viability of virus in the face of normal serum. The standard serum titration was included so that titrations of different sera carried out in separate tests could be standardised. The standard serum was stored at 4°C as vacuum-sealed ampoules of freeze-dried material and reconstituted with sterile distilled water to its original volume when required. The titration was carried out using 3-fold dilutions and the titre against $10^{1.9}$ to $10^{2.1}$ rabbit infective doses of lapinised rinderpest virus was $10^{2.0}$. Five days after inoculation the rabbits were killed and examined for the presence or absence of lessons of lapinised rinderpest virus infection (Fukusho and Nakamura, 1940). Rabbits which died before the fifth day after inoculation were likewise examined. If lesions were present the animal was included in the estimation of the titre. The few animals which died without lesions were excluded. The dilution of serum or whey at which 50 per cent. of the inoculated rabbits were infected was calculated using Thompson's method (1947) and the results expressed as the reciprocal logarithm to the base 10. The results were standardised by reference to the standard serum; for example, if the titre of this serum in a test was $10^{1.8}$ then 0.2 was added to all results of unknown sera titrations in the same test, whereas if the standard serum titre was $10^{2.2}$, 0.2 was subtracted from all titres. Where sera were expected to have either little or no detectable neutralizing antibody, they were tested at a dilution of 1:2; if all rabbits were found to be infected the titre was expressed as "nil", if 3 or 4 rabbits were infected the serum was considered to have a titre of <0.3 and if only 1 or 2 rabbits were infected the serum was titrated in the normal way. The sera of the immune dams of the vaccinated calves were screened by inoculating 3 rabbits with a serum-virus mixture in which the serum dilution was 1:20. If none of the rabbits was infected the animal was considered to be immune.

RESULTS

ACTIVE RINDERPEST IMMUNIZATION OF CALVES, THE PROGENY OF SUSCEPTIBLE DAMS

The immune response of calves, the progeny of rinderpest susceptible dams, and of adult cattle, to the inoculation of lapinized rinderpest virus is recorded in table 2.

None of the dams of the calves possessed detectable rinderpest neutralizing antibodies.

Differences between the titres of rinderpest neutralizing antibodies, 21 days after inoculation, produced by calves aged from 1 day to two months at the time of inoculation, and those of adult cattle were not significant ($t = 0.7662$, $P > 0.05$).

A brief note on preliminary findings on the production of rinderpest neutralizing antibodies by very young calves has been published (Brown, 1956).

TABLE 2

The Production of Rinderpest Neutralizing Antibodies by Calves, the Progeny of Susceptible Dams, and by Adult Cattle, following Lapinized Rinderpest Virus Inoculation.

Cattle No.	Age at Inoculation	Titre of Rinderpest Neutralizing antibodies expressed as the reciprocal of the logarithm of the 50% end-point dilution	
		Pre-Inoculation	21 days post-Inoculation
N2	1 day	Nil	1.8
K1	1 day	Nil	3.2
N4	4 days	Nil	2.9
N5	5 days	Nil	2.7
N7	5 days	Nil	2.3
N6	6 days	Nil	2.7
N11	29 days	Nil	2.5
K10	31 days	Nil	3.1
K12	63 days	Nil	2.8
2974	2 years	Nil	2.4
2975	2 years	Nil	2.4
2979	2 years	Nil	2.4
2981	2 years	Nil	2.9
2982	2 years	Nil	3.1

THE MODE OF TRANSFER OF MATERNALLY-DERIVED ANTIBODIES AND THEIR HALF-LIFE IN CALVES

The rinderpest neutralizing antibody titres of the sera of calves, the progency of immune dams, before and at various periods after suckling, together with the dams' sera at the time of calving, and their colostral wheys are given in table 3.

None of the calves' sera taken before suckling contained detectable rinderpest neutralizing antibodies. Antibody titres of the dams' sera at calving, the calves' sera after suckling, the colostral wheys, and milk taken at various periods after calving are given in table 4. The mean titres of the dams' sera at calving, the calves' sera after suckling, the colostral wheys, and milk taken at 30-48 hours, 1 week and 2 weeks after birth were 2.4, 2.8, 3.3, 1.6, 1.4 and 0.8 respectively.

Significant differences were found between the titres of the colostral wheys and the sera of calves after suckling ($t = 3.424$, $P < 0.01$), the colostral wheys and dams' sera ($t = 6.770$, $P < 0.01$) and the calves' and the dams' sera ($t = 2.530$, $P < 0.05$).

The ratios of the titres of the colostral whey to the dam's serum at calving, the calf's titre after suckling to the colostral whey and the calf's serum to the dam's serum recorded in table 5 had means of 7.2, 0.45 and 3.8 respectively.

No significant relationships were found between the titres of the colostral wheys and the dams' sera at calving ($F = 0.03$, $P > 0.05$) the colostral wheys and the calves' sera after suckling ($F = 0.09$, $P > 0.05$) or the dams' sera at calving and calves' sera after suckling ($F = 1.49$, $P > 0.05$).

The titres of rinderpest antibodies present in the sera of calves, after ingestion of colostrum from immune dams, were linear on time and the regressions were significant (table 6).

The regression lines of the fall of titre with time calculated from the titres recorded in table 10 of the sera of the 65 calves from immune dams, bled when aged 1 day to 12 months, and of calves numbers 1592, 1722, 420, 421, 422, 425 and 433 are given in table 6 and figures 1-8.

When the regression lines of the titres of calves 1592, 1722, 420, 421, 422, 425 and 433 were each compared with the line constructed from the titres of the sera of 65 calves, it was found that the differences were not significant (table 7).

The half-lifes of maternally-derived rinderpest neutralizing antibodies and the extinction points, calculated from the regression lines are given in table 8. The mean half-life was 36.7 ± 4.8 days and the mean extinction point 10.9 ± 1.1 months (1 month = 30 days). The extinction point was the calculated age after birth when the serum titre of maternally-derived rinderpest neutralizing antibody would have fallen to a titre of 0.0.

TABLE 3

Titres of Rinderpest Neutralizing Antibodies, Expressed as the Reciprocals of the Logarithms of the 50 per cent. end-point dilutions, of the Sera of Calves, the Progeny of Immune Dams, at Various Periods after Birth, together with those of their Dams' Sera and Colostral Wheys

DAM No.	1131	199	221	212	240	219	203
CALF No.	1592	1722	420	421	422	425	433
Titres of: Dam's serum at calving -	2.1	2.0	2.6	2.6	2.2	2.4	2.6
Colostral Whey	Not available	3.3	3.4	3.2	3.3	3.6	3.0
Serum of calf: Before suckling	Not available	NIL	NIL	NIL	NIL	NIL	NIL
30-48 hours after suckling	2.8	3.0	2.9	2.3	2.7	3.0	3.1
1 month of age	2.7	2.4					2.3
2 months	2.4					2.5	
3 months	1.9	2.0	1.5	2.1			
4 months	1.6				1.3		1.6
5 months	1.9					1.3	
6 months	1.8	1.2	0.8	1.2			
7 months	1.2						0.6
8 months	0.7	0.6	<0.3		<0.3	0.7	<0.3
9 months	<0.3			<0.3			
10 months	<0.3	<0.3	<0.3		0.3		NIL
11 months		NIL	<0.3	<0.3	NIL	<0.3	
12 months				NIL		<0.3	

TABLE 4

Rinderpest Neutralizing Antibody Titres, expressed as the Reciprocals of/the 50 per cent. /the logarithm of Neutralizing End-point, of the Sera, Colostral and Milk Wheys taken at Various Periods after Calving, of Rinderpest Immune Cows and their Calves.

	CALF NO.					
TITRE	420	421	422	425	433	1722
Serum of Dam at Calving	2.6	2.6	2.2	2.4	2.6	2.0
Calf's Serum 30-48 hrs. after birth	2.9	2.3	2.7	3.0	3.1	3.0
Colostral Whey	3.4	3.2	3.3	3.6	3.0	3.3
Milk Whey after calving:						
30-48 hrs.	-	2.1	-	-	1.2	-
1 week	-	1.3	-	-	1.6	-
2 weeks	-	0.6	-	-	1.0	-

TABLE 5

Colostral Whey Titre/Dam's Serum Titre at Calving, Calf's Serum Titre after suckling/Colostral Whey Titre and Calf's Serum Titre/Dam's Serum Titre Ratios

	Calf Number					
Ratio:	420	421	422	425	433	1722
Colostral Whey/ Dam's Serum	6.3	4.0	12.6	15.8	2.5	20.0
Calf's Serum/ Colostral Whey	0.32	0.13	0.25	0.25	1.26	0.50
Calf's Serum/ Dam's Serum	2.0	0.5	3.2	4.0	3.2	10.0

TABLE 6

FALL OF TITRE WITH TIME OF NATURALLY-ACQUIRED PASSIVE RINDERPEST IMMUNITY

Calf No.	Regression Line Formula	F
65 calves	$\hat{Y} = 2.7 - 0.25.X$	338.24^{**}
1592	$\hat{Y} = 2.9 - 0.26.X$	139.25^{**}
1722	$\hat{Y} = 2.8 - 0.26.X$	384.00^{**}
420	$\hat{Y} = 2.5 - 0.23.X$	29.69^{**}
421	$\hat{Y} = 2.5 - 0.21.X$	158.33^{**}
422	$\hat{Y} = 2.5 - 0.25.X$	79.00^{**}
425	$\hat{Y} = 2.8 - 0.23.X$	62.80^{**}
433	$\hat{Y} = 2.8 - 0.30.X$	121.00^{**}

TABLE 7

The Significance of Differences between the Slopes of the Regression Lines of Antibody Titre on Time between Individual Calves and the line constructed from 65 Calves from Immune Dams, each bled once when aged between 3 days and 1 year.

Calf No.	Slope	Correlation Coefficient	t	p
65 Calves	-0.25	0.922		
1592	-0.26	0.966	1.155	<0.3>0.2
1722	-0.26	0.924	0.025	>0.9
420	-0.23	0.944	0.288	<0.8>0.7
421	-0.21	0.980	1.174	<0.3>0.2
422	-0.24	0.974	0.783	<0.5>0.4
425	-0.23	0.977	1.054	<0.3>0.2
433	-0.30	0.988	1.611	<0.2>0.1

TABLE 8

HALF-LIFES AND EXTINCTION PERIODS OF MATERNALLY-DERIVED RINDERPEST NEUTRALIZING ANTIBODIES IN CALVES

Calf No.	Half-Life of Antibody in days	Extinction Point* in months**
65 calves	36	10.6
1592	34.5	11.2
1722	34.5	10.8
420	39	10.8
421	42.9	11.7
422	37.5	10.4
425	39	12.2
423	30	9.3
Mean	36.7	10.9

*Extinction Period was the time calculated for the titre to fall to 0.0.

**1 Month = 30 days.

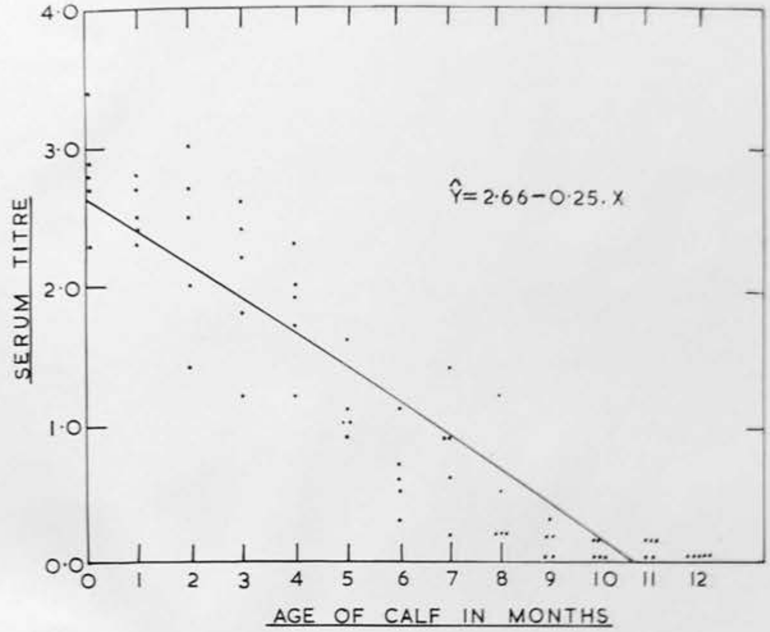

FIG. 1: THE DURATION OF NATURALLY-ACQUIRED PASSIVE IMMUNITY TO RINDERPEST CALCULATED FROM THE TITRES OF 65 CALVES

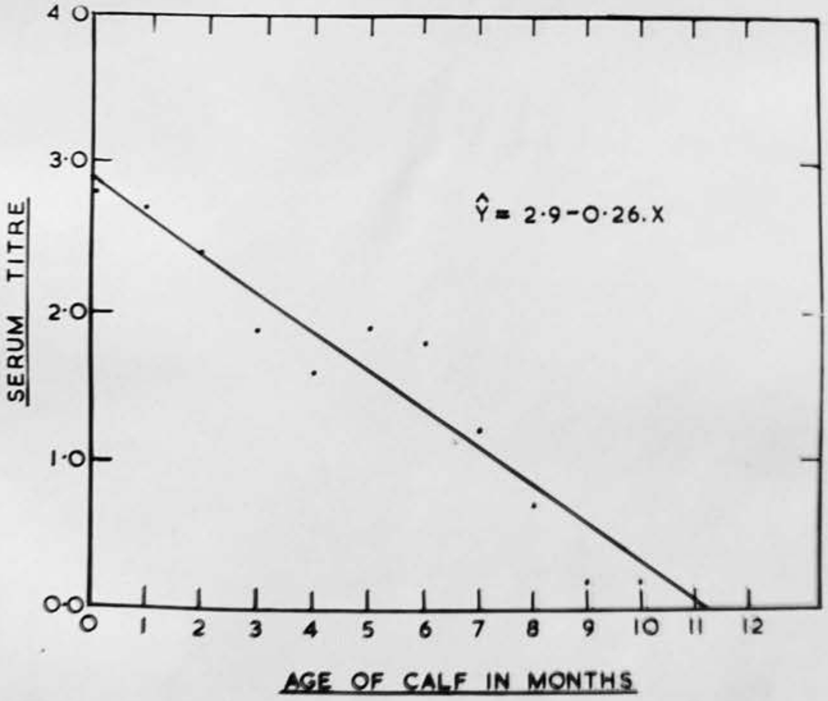

FIG. 2: THE DECLINE OF NATURALLY-ACQUIRED PASSIVE IMMUNITY TO RINDERPEST IN CALF 1592

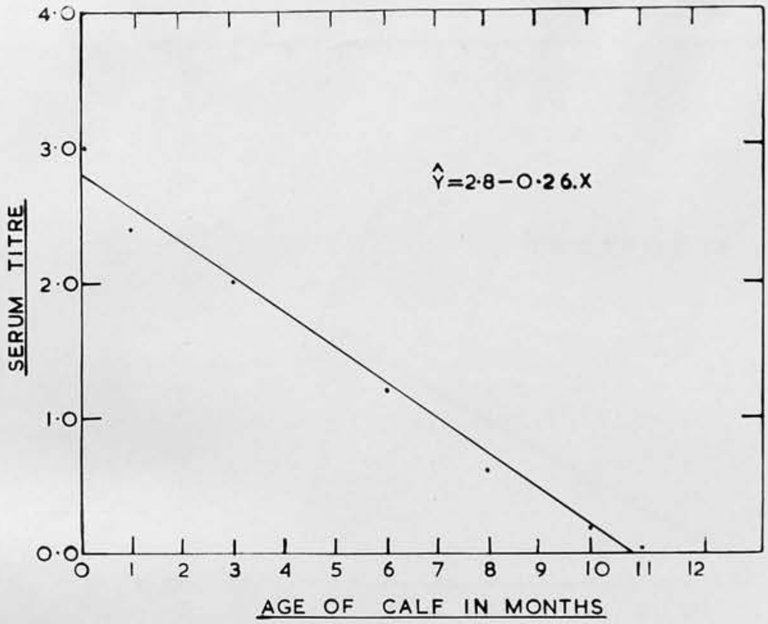

FIG. 3: THE DECLINE OF NATURALLY-ACQUIRED PASSIVE IMMUNITY TO RINDERPEST IN CALF 1722

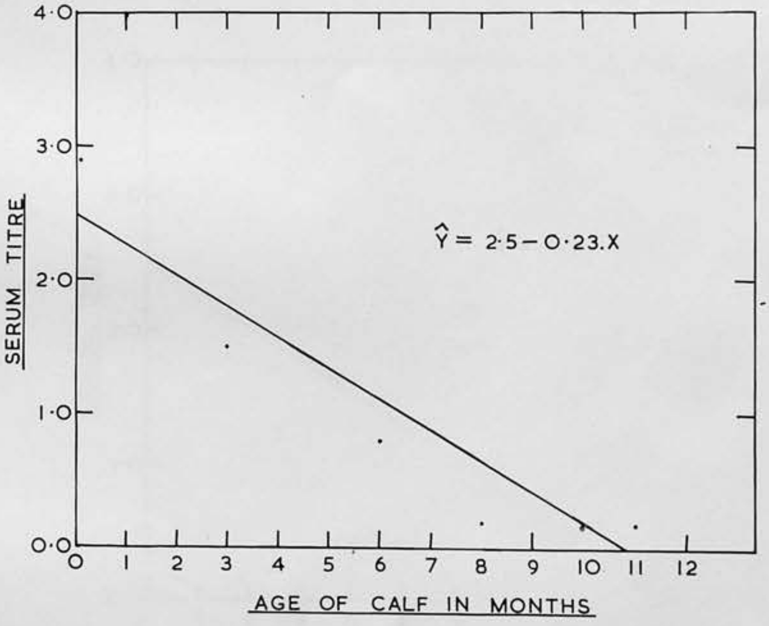

FIG. 4 : THE DECLINE OF NATURALLY- ACQUIRED PASSIVE IMMUNITY TO RINDERPEST IN CALF 420

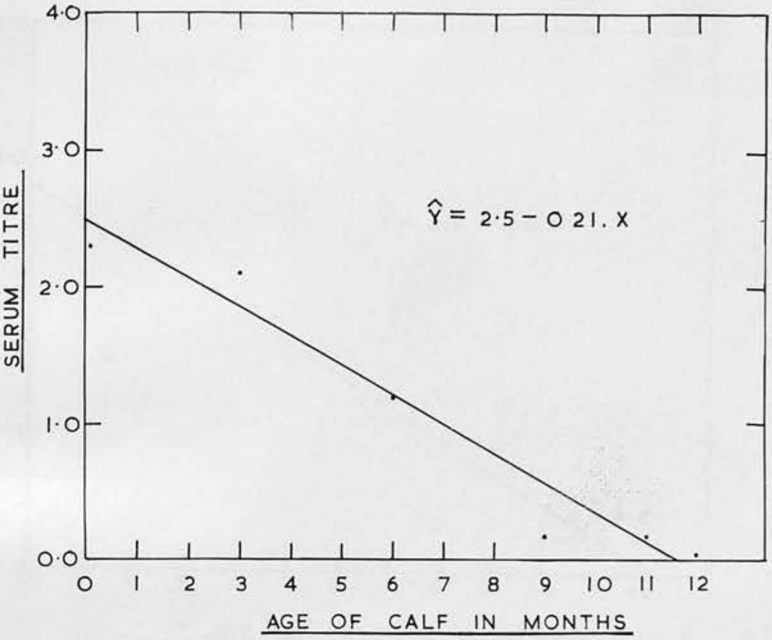

FIG. 5: THE DECLINE OF NATURALLY-ACQUIRED PASSIVE IMMUNITY TO RINDERPEST IN CALF 421

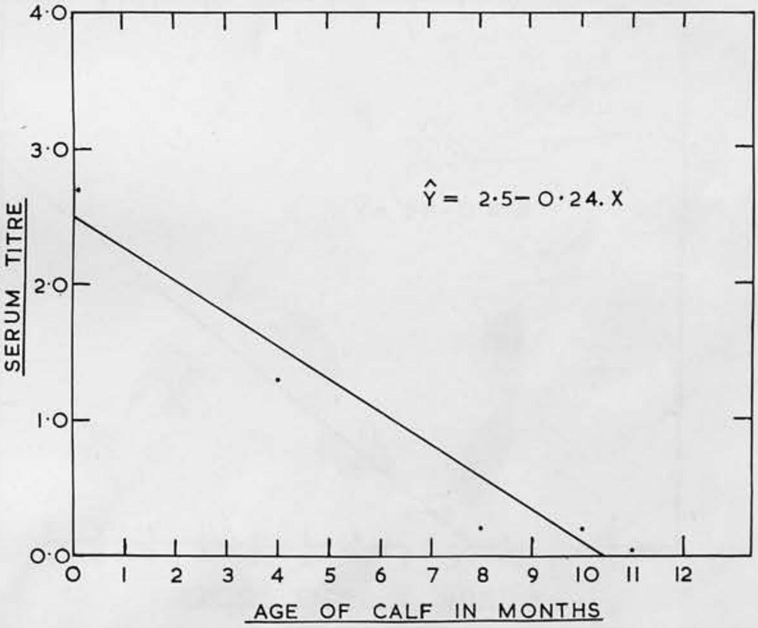

FIG. 6: THE DECLINE OF NATURALLY-ACQUIRED PASSIVE IMMUNITY TO RINDERPEST IN CALF 422

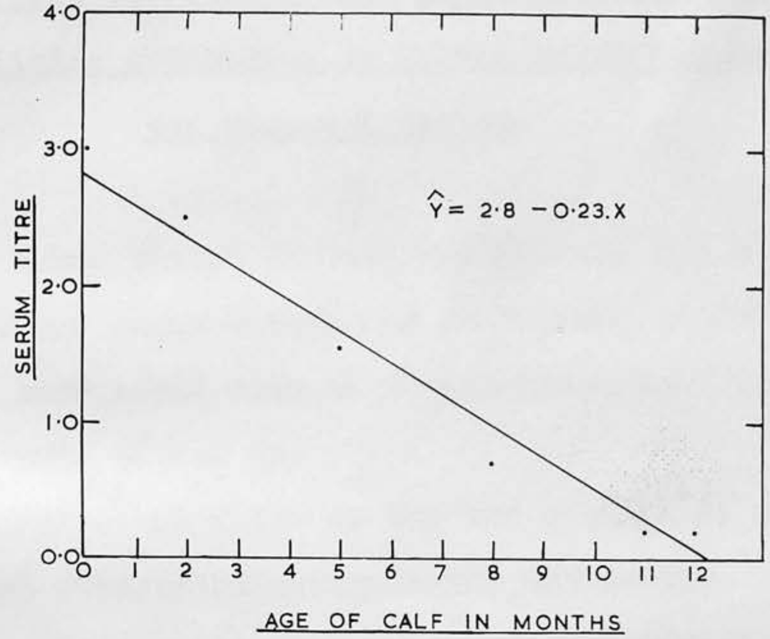

FIG. 7: THE DECLINE OF NATURALLY–ACQUIRED PASSIVE IMMUNITY TO RINDERPEST IN CALF 425

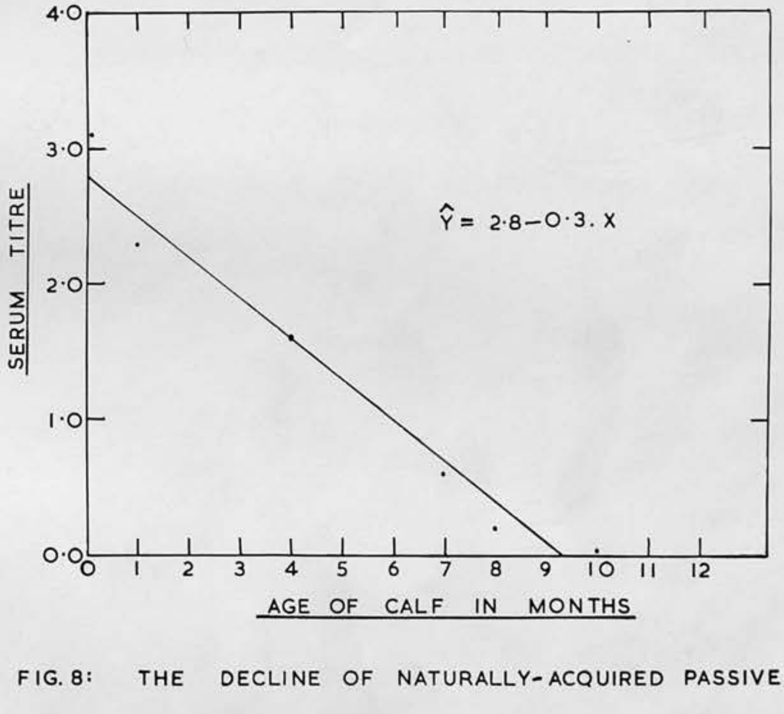

FIG. 8: THE DECLINE OF NATURALLY-ACQUIRED PASSIVE IMMUNITY TO RINDERPEST IN CALF 433

The Effect of Feeding Milk Containing Rinderpest Neutralizing Antibodies to Calves which had passed the Neonatal Period.

The serum titres of dams and calves, and of colostral and milk wheys taken before and at various periods after 2 dams were inoculated with lapinized rinderpest virus are given in table 9A and 9B.

The colostral wheys of the two rinderpest susceptible dams lacked rinderpest neutralizing antibodies.

Rinderpest antibodies were present in milk wheys from the dams at 7 days but not at 4 days after the inoculation of lapinized rinderpest virus. Therefore although the 2 calves each ingested 1 gallon of its dam's milk, which contained rinderpest antibodies, daily for a period of 5 weeks when aged between 8 and 43 days, at no time did the calves possess detectable rinderpest antibodies in their sera. This indicated that absorption of antibody from the gut did not occur.

TABLE 9A

Rinderpest Neutralizing Antibody Titres of the Sera, Colostral and Milk Wheys from Cow No.K20, and Sera from her Calf, before and after the Dam was inoculated with Lapinized Rinderpest Virus. The Calf ingested 1 gallon of its Dam's Milk daily during the first 43 days after birth

Time	Rinderpest Neutralizing Antibody Titre* of:		
	Dam's Serum	Dam's Colostral or Milk Whey	Calf's Serum
3 hours after calving	–	NIL (Colostrum)	–
1 day after calving. Dam inoculated with Lapinized Rinderpest Virus	NIL	NIL (Milk)	NIL
4 days after inoculation	–	NIL (Milk)	–
7 " " "	–	0.9 "	NIL
14 " " "	–	0.9 "	NIL
21 " " "	2.2	–	NIL
42 " " "	–	0.8 "	NIL

*Expressed as the reciprocal of the logarithm of the 50 per cent. neutralizing dilution.

TABLE 9B

Rinderpest Neutralizing Antibody Titres of the Sera, Colostral and Milk Wheys from Cow No.K21, and Sera from her Calf, before and after the Dam was inoculated with Lapinized Rinderpest Virus. The Calf ingested 1 gallon of its Dam's Milk daily during the first 43 days after Birth

Time	Rinderpest Neutralizing Antibody Titre*of:		
	Dam's Serum	Dam's Colostral or Milk Whey	Calf's Serum
3 hours after calving	–	NIL (Colostrum)	–
1 day after calving. Dam inoculated with Lapinized Rinderpest Virus	NIL	NIL (Milk)	NIL
4 days after inoculation	–	NIL (Milk)	–
7 " " "	–	0.5 (Milk)	NIL
14 " " "	–	0.9	NIL
21 " " "	2.6	–	NIL
42 " " "	–	0.9	NIL

*Expressed as the reciprocal of the logarithm of the 50 per cent. neutralizing dilution.

ACTIVE RINDERPEST IMMUNIZATION OF CALVES, THE PROGENY OF IMMUNE DAMS

Preinoculation, 21 day and 1 year post-inoculation serum titres of rinderpest neutralizing antibodies and clinical reactions of calves, the progeny of immune dams, inoculated with caprinized rinderpest vaccine (K.A.G.) are recorded in table 10.

All the dams of those calves which possessed no detectable rinderpest neutralizing antibodies at the time of inoculation were found to be immune.

Those calves which possessed no detectable rinderpest antibodies 1 year after inoculation were considered not to have been actively immunized following the caprinized rinderpest virus inoculation. Thus the 1 year post-inoculation serum titres of the calves indicated that no calf aged 3 months or less at the time of inoculation produced antibodies. On the other hand, all calves inoculated when aged 8 months or more were actively immunized. Some of the calves aged from 4-7 months were, and others were not, immunized. Some of the calves which possessed maternally-derived antibodies at the time of K.A.G. inoculation, were actively immunized.

All calves which had a preinoculation titre of 0.7 or less produced antibodies whereas no calf did so which had a preinoculation titre of 2.2 or greater. The response of those calves possessing preinoculation titre between these two levels varied.

The amount of antibody produced during the 21 days following inoculation was calculated by subtracting the preinoculation titre from the post-inoculation titre and, with those calves in which antibodies were present before inoculation, adding 0.2 to the result. The 0.2 was added because this was approximately the amount by which the preinoculation titre would have fallen during 21 days, the half-life being about 37 days.

In those instances where calves were actively immunized following inoculation with caprinized rinderpest virus, the following were found:

(a) There was a significant relationship between the preinoculation titre and the amount of antibody produced during the 21 days after inoculation ($r = -0.7136$, $P < 0.001$). Where the preinoculation titre was low or absent, the amount of antibody produced was large; conversely where the preinoculation titre was high the amount of antibody produced was low.

(b) There was a significant relationship between the preinoculation titre and the 1 year post-inoculation titre ($r = -0.5554$, $P < 0.001$). In those calves which had little or no maternally-derived antibody at the time of inoculation, the 1 year post-inoculation titres were higher than in those calves in which the preinoculation titres were high.

(c) There was a significant regression of the amount of antibody produced during the 21 days following inoculation on the age of calf at the time of inoculation ($\hat{Y} = -1.1+0.38.X$, $t = 8.216$, $P < 0.001$).

(d) There was a significant regression of the 1 year post-inoculation titre on the age of the calf at the time of inoculation ($\hat{Y} = 0.9 + 0.17.X$, $t = 3.356$, $P < 0.02 > 0.01$).

The mean preinoculation and 1 year post-inoculation titres of rinderpest antibody and the titre of antibody produced during the 21 days after inoculation, of those calves, of various age groups, which were actively immunized following caprinized rinderpest virus inoculation, are recorded in table 11.

Findings on maternally-derived passive immunity and active immunity to rinderpest in calves from immune dams, are summarized diagrammatically in figure 9.

The immune response of calves, from immune dams, to the inoculation of lapinized rinderpest virus 12-15 months after the ineffective inoculation of caprinized rinderpest virus is recorded in table 12.

TABLE 10

The response of calves aged from 2 days to 1 year, the progeny of immune dams, to Caprinized rinderpest vaccine, the serum titres of rinderpest neutralizing antibody being expressed as the reciprocal of the logarithm of the 50% end-point dilution

Age Group	Calf	Age at Inoculation in days	Post-Inoculation Thermal Reaction	Pre-Inoculation Titre	Post-Inoculation Titre	
					21 days	1 year
2 - 6 days	462 ♀	3	-	2.3	2.3	NIL
	463 ♀	3	-	2.9	3.1	NIL
	464 ♀	6	-	3.4	2.9	NIL
	466 ♀	2	-	2.8	2.6	NIL
	468 ♀	3	-	2.7	2.0	NIL
1 month (30 days)	457 ♀	29	-	2.7	2.0	NIL
	458 ♀	28	-	2.3	2.0	NIL
	459 ♂	28	-	2.8	2.8	NIL
	460 ♂	33	-	2.4	2.4	NIL
	461 ♂	28	-	2.5	2.2	NIL
2 months (61 days)	452 ♀	64	-	2.7	2.0	NIL
	453 ♂	61	-	3.0	2.3	NIL
	454 ♀	59	-	2.0	2.0	NIL
	455 ♀	59	-	1.4*	1.5	NIL
	456 ♀	58	-	2.5	2.3	NIL

TABLE 10 CONTINUED

Age Group	Calf	Age at Inoculation in days	Post-Inoculation Thermal Reaction	Pre-Inoculation Titre	Post-Inoculation Titre	
					21 days	1 year
3 months (91 days)	447 ♀	89	-	2.4	1.8	NIL
	448 ♀	88	-	1.2	1.2	NIL
	449 ♀	91	-	2.6	1.9	NIL
	450 ♀	88	-	2.2	1.9	NIL
	451 ♂	87	-	1.8	1.2	NIL
4 months (122 days)	442 ♂	123	-	2.0	1.8	1.9
	443 ♂	123	-	1.9	1.8	NIL
	444 ♂	123	-	1.2	1.3	NIL
	445 ♀	122	-	1.7	1.1	NIL
	446 ♀	121	-	2.3	2.0	NIL
5 months (152 days)	437 ♀	155	-	1.1	1.2	NIL
	438 ♀	154	-	1.0	1.3	1.9
	439 ♀	153	-	1.0	1.7	2.3
	440 ♀	153	+	0.9	2.3	2.3
	441 ♀	152	-	1.6	1.3	1.8
6 months (182 days)	431 ♀	186	-	0.6	1.8	2.4
	432 ♀	181	+	0.5	2.6	2.2
	434 ♂	180	+	0.7	2.6	2.4
	435 ♂	182	-	0.3	2.0	1.4
	436 ♀	179	-	1.1	1.7	1.6

TABLE 10 CONTINUED

Age Group	Calf	Age at Inoculation in days	Post-Inoculation Thermal Reaction	Pre-Inoculation Titre	Post-Inoculation Titre	
					21 days	1 year
7 months (213 days)	426 ♀	210	++	<0.3	2.8	2.5
	427 ♀	209	−	0.9	1.0	1.9
	428 ♂	208	−	0.9	1.0	NIL
	429 ♂	208	−	1.4	1.2	1.9
	430 ♂	207	+	0.6	2.0	2.4
8 months (243 days)	319 ♂	243	+	<0.3	2.4	2.9
	417 ♂	246	++	<0.3	2.5	2.4
	418 ♀	243	+	0.5	2.5	2.5
	419 ♀	244	+	<0.3	2.5	1.8
	423 ♂	242	+	1.2	2.6	2.3
9 months (274 days)	294 ♂	271	+	<0.3	2.7	2.0
	295 ♂	273	+	0.3	2.8	2.5
	313 ♂	270	+	NIL	2.6	2.7
	314 ♀	276	+	NIL	2.8	2.4
	318 ♂	278	+	<0.3	2.6	2.4
10 months (304 days)	288 ♀	313	++	<0.3	2.5	2.3
	289 ♀	312	+	NIL	2.8	2.7
	290 ♂	310	++	NIL	3.4	2.8
	291 ♀	309	+	NIL	2.8	2.6
	292 ♀	309	++	<0.3	3.0	2.9

TABLE 10 CONTINUED

Age Group	Calf	Age at Inoculation in days	Post-Inoculation Thermal Reaction	Pre-Inoculation Titre	Post-Inoculation Titre	
					21 days	1 year
11 months (334 days)	273 ♀	343	++	NIL	3.0	2.6
	275 ♀	340	++	<0.3	3.3	2.9
	277 ♀	340	+	<0.3	3.3	2.4
	278 ♀	339	+	<0.3	3.2	2.2
	279 ♀	338	+	NIL	2.5	Died*
12 months (365 days)	263 ♀	375	++	NIL	3.3	2.7
	264 ♂	375	++	NIL	2.8	1.9
	269 ♀	359	++	NIL	2.9	2.5
	270 ♂	364	+	NIL	3.0	2.7
	271 ♀	363	+	NIL	3.4	2.7

\+ Thermal Reaction

++ Thermal Reaction together with diarrhoea following K.A.G. inoculation

\- No Thermal Reaction following K.A.G. inoculation

* Died from acute rimenal tympany 11 months after inoculation

TABLE 11

The mean preinoculation and 1 year post-inoculation serum titres of rinderpest neutralizing antibody and the titre of antibody produced during the 21 days after inoculation, of those calves, of various age groups, which were actively immunized following caprinized rinderpest virus inoculation.

Age Group	No. of observations	Mean titre*		
		Pre-inoculation	Antibody produced during 21 days after inoculation	1 year post-inoculation
12	5	NIL	3.1	2.5
11	5	0.2	3.0	2.5
10	5	0.1	2.9	2.7
9	5	0.2	2.7	2.4
8	5	0.5	2.2	2.4
7	4	0.8	1.2	2.2
6	5	0.6	1.7	2.0
5	4	1.1	0.8	2.1
4	1	1.8	0	1.9

*Expressed as the reciprocal logarithm base$_{10}$ of the 50 per cent. neutralizing dilution.

TABLE 12

The Immune Response of Calves, from Immune Dams, to Lapinized Rinderpest Virus 12-15 Months after the Ineffective Inoculation of Caprinized Rinderpest Virus

Calf No.	Age at Time of Caprinized Rinderpest Virus Inoculation	Age at Time of Lapinized Rinderpest Virus Inoculation	Serum Titre* of Rinderpest Neutralizing Antibodies		
			Pre-Inoculation	4 days Post-Inoculation	21 days Post-Inoculation
428	7 months	20 months	NIL	NIL	2.9
437	5 "	17 "	NIL	NIL	2.8
443	4 "	17 "	NIL	NIL	2.5
447	3 "	17 "	NIL	NIL	2.6
457	1 month	16 "	NIL	NIL	2.6
462	3 days	15 "	NIL	NIL	2.6

*Expressed as the reciprocal of the logarithm of the 50 per cent. neutralizing dilution.

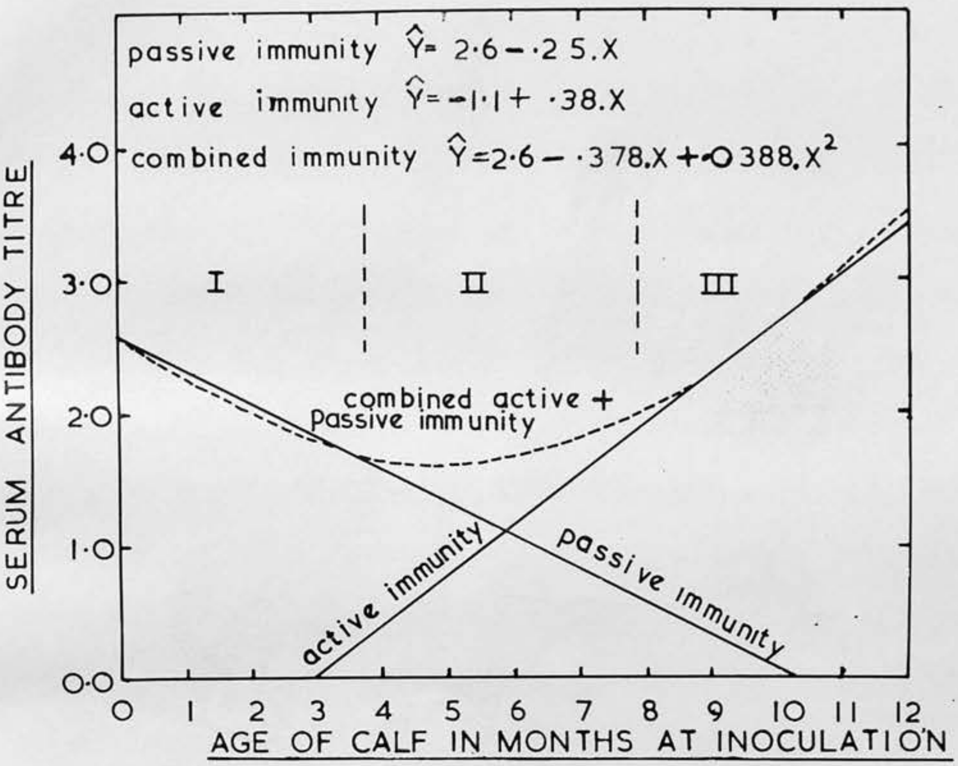

FIG. 9 THE RESPONSE OF CALVES FROM RINDERPEST-IMMUNE DAMS TO CAPRINIZED RINDERPEST VIRUS INOCULATION

PERIOD I NO CALVES IMMUNIZED
PERIOD II SOME " "
PERIOD III ALL " "

ACTIVE IMMUNITY= antibody produced during 21 days following virus inoculation

DISCUSSION

The conclusions drawn from the experiments on rinderpest immunity in calves, detailed in this thesis, are based on the hypothesis that there is a relationship between rinderpest neutralizing antibodies in the serum and the state of immunity of the animal. Cattle which were susceptible to challenge with bovine rinderpest virus were found not to possess rinderpest neutralizing antibodies whereas those animals not susceptible to challenge possessed them. These antibodies appeared in the sera of cattle following immunization against rinderpest (Scott & Brown, 1957).

Hitherto the serological response of very young calves to viable viral antigens has not been ascertained. We found that day-old calves responded to lapinised rinderpest virus just as well as adults. This result is comparable to that obtained with skin homographs, which induced vigorous reactions following grafting onto day-old calves (Billingham and Lampkin, 1957). Trichomonas foetus, Brucella abortus and Salmonella dublin antigens behaved differently. (Kerr and Robertson, 1954; Kerr, 1956). We might suggest that apparent failures of very young calves to produce antibodies following the inoculation of bacterial or protozoal antigens could be attributed to weaknesses in the techniques used to measure the responses. However, with Tr. foetus antigen at least, this objection is not valid, for not only were calves of under the age of 1 month unable to produce agglutinins but 3 calves of 23 or less days of age acquired a tolerance to the antigen as shown by an impairment of the ability of the calves to respond to further antigenic stimulus (Kerr and Robertson, 1954). Development of tolerance necessarily implies an inability to produce antibodies.

We can only conclude therefore that a period of immunological immaturity occurs in calves after birth, but this immaturity only relates to some, but not all antigens. The concept that very young calves may produce antibodies against one antigen but not against another is not revolutionary. Some skin homographs exchanged between very young chicks survived for long periods, but all chicks aged 2 weeks or more at the time of transplantation rapidly rejected the homographs (Cannon and Longmire, 1952). However, Wolfe and Dilks (1948) found that the proportion of chicks which produce precipitins to bovine serum did not reach 100 per cent until 5 week old birds were used.

We are unable to say with absolute certainty that there is not a period of immunological immaturity in very young calves, so far as viable lapinised rinderpest virus antigen is concerned, because the calves were bled and the sera titrated 3 weeks after inoculation. If such a period of immaturity exists it must be 7 days or less because a period of 2 weeks is necessary for the rinderpest neutralizing antibody titre of serum to reach its maximum in adult cattle following lapinized rinderpest virus inoculation

(MacOwan, 1956; Scott, 1956).

Whether calves in utero can form antibodies is not known.

The finding that young calves of all ages between 1 and 63 days from rinderpest-susceptible dams produced neutralizing antibodies following the inoculation of lapinised rinderpest virus confirms Gillain's (1945) view that difficulties associated with immunizing some young calves against rinderpest are not due to an age factor.

Bacterial, protozoal, antitoxin and rickettsial antibodies have been found to be transmitted from immune cows to their calves via the colostrum. The route of transfer of foot and mouth disease antibodies was the same (Schneider, 1955). Similarly we found that maternally-derived rinderpest antibodies were transmitted to the calf by the colostrum as calves born of immune dams lacked antibodies at birth but possessed them to a high titre 30-48 hours after suckling. This finding supports previous rinderpest workers who assumed that maternally-derived rinderpest antibodies were transmitted through the colostrum and refutes the suggestion of Rabagliati (1924) and Gillain (1944) that calves possess rinderpest antibodies at birth.

The statement of Hale, Walker, Maurer, Baker and Jenkins (1946) that "no immunity is conferred to calves born of (rinderpest) vaccinated animals" is clearly incorrect.

In our experiments all calves born of immunized dams were passively immunized following ingestion of colostrum. Contrary to the view of Rabagliati (1924) we found that the serum titre of a calf (NO.1592) after suckling, born of a dam immunized during pregnancy, did not differ from those of calves born of dams immunized before pregnancy.

Our findings that the colostral whey antibody titres were higher than the dams' serum titres, and that the serum titres of the calves shortly after suckling were less than those of the colostral whey but greater than those of the dams' sera, are similar to results previously obtained with other antigen-antibody systems. The number of our observations was too small to allow finding significant relationships.

Secretion of antibodies by the bovine mammary gland did not end when all the colostrum had been ingested by the calf for two weeks after calving, rinderpest neutralizing antibodies were present in the milk of immune dams, but in a titre of about one hundredth of that of the colostrum at the time of calving.

After the calves ingested immune colostrum the titres of maternally-derived rinderpest antibodies in the serum declined linearly with time. This is similar to results obtained previously with diphtheria antitoxin in babies (Barr _et al_. 1949) and lambs (Barr _et al_. 1953), and with lamb dysentery antitoxin in lambs (Mason _et al_. 1930).

The mean extinction point/period of maternally-derived rinderpest neutralizing antibodies in calves was 10.9 months. This period is similar to that reported for diphtheria antitoxin in babies (Neill *et al*. 1932; Barr *et al*. 1949) but exceeds that of up to 6 months found, for example, with maternally-derived *Br. abortus* agglutinating antibodies in calves (McAlpine and Rettger, 1925; Thorp & Graham, 1933; McDiarmid, 1946), *Salmonella abortus-equi* agglutinating antibodies in foals and *Corynebacterium diphtheriae* agglutinating antibodies in human infants. As with differences between the production of rinderpest neutralizing antibodies and protozoal agglutinating antibodies by very young calves, one might suggest that a possible explanation of differences could be a lack of sensitivity in the techniques used to determine the presence of bacterial antibodies. Such a suggestion is not unreasonable. A possibly allied phenomenon is the disappearance of complement-fixing antibodies for rinderpest from the sera of cattle within 6 months of infection (Cooper, 1946) while the animals concerned remained immune, whereas rinderpest neutralizing antibodies have been found to persist in cattle for as long as 13 years after immunization with caprinised rinderpest vaccine (Brown and Rashid, 1957). However, this suggestion that differences in the period of persistence of maternally-derived antibodies may be explained by variations of sensitivity in the tests used is difficult to support, because maternally-derived distemper neutralizing antibodies persisted for not longer than 3 months after birth in pups (Gillespie, 1956) and 6 months in human infants (Karzon, 1955). These antibodies were detected and measured by means of neutralization tests which one might reasonably expect to be as sensitive as those used to determine the presence of diphtheria antitoxin and rinderpest antibodies.

Whether there are any other factors, apart from the amount of antibody which the young animal receives from its mother, which produce variations in the period of persistence of maternally-derived antibodies is unknown.

The mean half-life of maternally-derived rinderpest antibody was 36.7 days. This figure is similar to results obtained by other workers for diphtheria antitoxin in lambs (Barr _et al_. 1953) and human infants (Barr _et al_. 1949). The half-life of rinderpest antibody in calves was calculated without reference to the dilution of antibody by the growth of the calves. Attempts to apply the formula of Wiener (1949) for calculating the half-life of maternally-derived antibody while allowing for dilution by growth of the animal gave unsatisfactory results as the variation was markedly increased. We were unable to find any references on the changes of serum volume of calves with growth, and without this information the true half-life of maternally-derived rinderpest antibody in calves cannot be calculated.

The half-life of passively and artificially-acquired rinderpest antibodies in cattle is unknown. In a single experiment a steer weighing 560 lb. was inoculated subcutaneously with 100 ml. of immune rinderpest serum having a titre of 3.2. Twenty-four hours after inoculation the serum titre of the steer was 0.7, but 14 days later no rinderpest neutralizing antibodies were detectable. If the half-life of inoculated rinderpest neutralizing serum antibody is the same as that of colostral antibody, antibodies should have been present for a period of up to about 2 months after inoculation. The reason for the discrepancy is unknown, and requires investigation.

We found no evidence to support the claim of Campbell, Sarwar and Petersen (1957) that effective absorption of antibody from the gastro-intestinal tract occurs after the neonatal period. Rinderpest antibodies were not detected at any time in the sera of two calves which, for a period of 5 weeks, consumed milk containing these antibodies. We realize that the number of calves used in the experiment was small. However, our findings received added support from the results of the experiments on the duration of maternally-derived rinderpest antibodies in calves. The serum titres declined linearly on time, which suggested that reinforcement of the passive immunity was not occurring although the calves were ingesting milk for periods of 6-9 months after birth. Nor does the claim of Campbell, Sarwar and Petersen accord with the evidence of Comline _et al_. (1951) and Hansen & Phillips (1947) who reported that absorption of antibody and gamma globulin from the gut of calves only occurred during the first few hours of life. A further objection, a theoretical one, can be postulated against the hypothesis of Campbell, Sarwar and Petersen. If the gut of the calf is permeable to protein molecules for a considerable time after the neonatal period, the animal might absorb, in addition to lactoglobulin, foreign proteins inducing hypersensitivity against a wide variety of antigens.

Because of the difficulties associated with the immunization of some young calves against rinderpest, a special procedure has been adopted in areas of East Africa where compulsory rinderpest vaccination is enforced. All cattle presented for immunization are inoculated but only those animals which, in the opinion of the field officer, are more than 12 months old are branded to show that they have been immunized. Cattle less than 12 months old are not branded and, by law, must be re-presented for vaccination in the following year. This practical policy is fully justified by our experimental findings because only calves of 8 months of age or greater, born of immune dams, were invariably immunized following the inoculation of caprinised rinderpest virus.

No calves of 3 months old or less from immune dams produced rinderpest antibodies while results in calves aged between 4 and 7 months old varied. Some calves which possessed maternally-derived rinderpest antibodies were actively immunized. The result depended upon the level of passive immunity. All calves in which the preinoculation serum titre was 0.7 or below produced antibodies whereas no calves in which the preinoculation titre was 2.2 or greater did so. Results in calves possessing a preinoculation serum titre which was between these two levels varied.

Where calves were actively immunized the preinoculation titre influenced the titres found 21 days and 1 year after inoculation. Where the preinoculation titre was high the amount of actively produced antibody was low. Conversely, where little or no maternally-derived antibody was present at the time of inoculation, the amount of antibody produced approached or equalled that produced by susceptible adult cattle. One year after K.A.G. virus inoculation, there were still significant differences between the titres of the calves inoculated at various ages. Those animals which had high titres 21 days after inoculation still had significantly higher titres than those in which the initial response was poor. However, the serum titres of actively produced antibody of this latter group had risen after the 21 day post-inoculation period; in many instances the 1 year post-inoculation titre was greater than the 21 day post-inoculation titre. Thus calves which possessed high preinoculation titres of maternally-derived rinderpest antibodies but which were actively immunized, produced antibodies at a slower rate than those calves which possessed little or no passive immunity before inoculation.

Many of the results obtained in the immunization of calves from immune mothers against rinderpest are similar to those obtained in the immunization against diphtheria of babies possessing maternally-derived antitoxin. Calves could produce antibody when possessing a passive immunity, as could babies. Also two levels of passive immunity were found to exist; all calves with tites below the lower level produced antibodies whereas none of those calves with titres above the higher limit did so. Also the amount of antibody produced and the rate of production depended upon the level of passive immunity existing at the time of inoculation. However our finding that these differences in the amount of antibody produced in the 21 days following inoculation were still reflected in the serum titres 1 year after inoculation differs somewhat from results obtained from work on diphtheria immunization. Greenberg and Fleming (1951) reported that 1 year after inoculation of diphtheria toxoid there was no significant difference between the average serum antitoxin titres of babies who lacked detectable diphtheria antitoxin at the time of inoculation and those who possessed it.

The finding that all calves which possessed maternally-derived rinderpest antibody to a titre of 0.7 or less produced antibody following K.A.G. inoculation is similar to results obtained by Scott (1956) in a different field. He investigated the effect of inoculating bovine rinderpest virus into cattle which previously had been actively immunized by the same virus strain. All cattle in which the antibody titre had fallen to 1.0 or less produced antibody following the second inoculation of virus. Scott used a neutralization test in which the serum virus mixtures containing 100 rabbit ID_{50} of lapinised rinderpest virus were held overnight at +4°C before inoculation into rabbits. No significant differences were found between results obtained when sera were titrated by this method and those obtained by the method used in the work described in this thesis (Scott and Brown, 1957).

Some of the calves from immune dams inoculated with K.A.G. virus produced antibodies without showing thermal reactions, thus confirming the finding of Rabagliati (1924). This finding suggests that Milne's (1955) view that maternally-derived rinderpest immunity in calves from immune dams may last as long as 19 months is probably incorrect. In his experiments a calf from an immune dam was inoculated with K.A.G. twice, the second time being when it was 19 months old. No thermal reaction occurred after either inoculation. Therefore, concluded Milne, the maternally-derived immunity was still present 19 months after birth. However, it seems probable that the calf was actively immunized when first inoculated without showing a thermal reaction.

Contrary to the findings of Milne (1955) we found that all calves which showed a thermal reaction following K.A.G. inoculation produced antibodies and were still immune 1 year later.

It is of interest to note that in our experiments all calves which showed signs of diarrhoea following caprinized rinderpest virus inoculation possessed little or no passive immunity.

Those calves which lacked rinderpest neutralizing antibodies in their sera 12-15 months after K.A.G. inoculation and which were then inoculated with lapinized rinderpest virus did not possess rinderpest antibodies in their sera 4 days after the latter inoculation. This indicated that in addition to the failure of the K.A.G. inoculation to stimulate the production of an active immunity, the antibody mechanism was not sensitized to rinderpest antigen, as Scott (1956) found that in cattle, where a secondary response to rinderpest antigen occurred, an increase in antibody titre was demonstrable 4 days after the second inoculation. Our results differ from those found in human infants (Osborn _et al_. 1952 b) and lambs (Barr _et al_. 1953) from diphtheria-immune mothers. In some instances where the maternally-derived immunity was considerable, although there was no active production of antitoxin following diphtheria toxoid inoculation, the antibody forming mechanismswere sensitized as shown by typical secondary responses following re-inoculation of the antigen.

Generally speaking our findings on rinderpest immunity in calves support the views of many field and laboratory workers. Since the work of Montgomery in 1915, much information has been obtained, although sometimes by means of uncertain experimental methods. One of the pioneers in the field, Croveri (1919), deduced many of the right answers to the problem from limited data. Our results have confirmed and extended some previous findings and put them on a more exact foundation.

SUMMARY

Rinderpest immunity in calves was investigated by a study of neutralizing antibodies.

In young calves aged from 1 day to 2 months, the progeny of rinderpest susceptible dams, the serological response to viable lapinized rinderpest virus, as measured by the serum titres 21 days after inoculation, did not differ from those of adult susceptible cattle.

Maternally-derived rinderpest antibodies were found to be transferred from the dam to the calf via the colostrum. No antibodies were detected in the sera of calves before suckling. The colostra of immune dams contained rinderpest antibodies to a higher titre than that of the dams' sera; 30-48 hours after the ingestion of such colostra, newborn calves possessed high antibody levels in their sera, levels greater than those of their dams' sera, approaching but less than those of the colostra ingested. Thereafter the antibody levels in the calves' sera declined linearly. The mean half-life of maternally-derived rinderpest antibody in calves was 36.7 days and the extinction point 10.9 months (the extinction point was the time calculated for the titre to fall to $10^{0.0}$, 1 month being equal to 30 days).

Two young calves, from susceptible dams, which each ingested daily for 5 weeks 1 gallon of milk containing rinderpest antibodies failed to show evidence of their absorption from the intestinal tract.

In calves which were the progeny of rinderpest-immune dams the serological response to viable caprinized rinderpest virus depended upon the level of maternally-derived passive immunity at the time of inoculation. All calves aged 8 months or more at the time of inoculation produced antibodies, whereas no calves aged 3 months or less did so. Some calves aged between 4 and 7 months were, and others were not, actively immunized. Two critical levels of maternally-derived antibodies occurred, one below which all calves produced antibodies and another above which no calf produced antibodies. The response in calves with preinoculation titres between these two levels varied. There was a significant relationship between the level of maternally-derived antibody at the time of inoculation of vaccine and the amount of antibody produced during the following 3 weeks, the greater the preinoculation titre the smaller the amount of antibody produced. Similarly there was also a significant relationship between the preinoculation titre and the 1 year post-inoculation titre. Also, where calves possessed a high level of antibody before inoculation, but were actively immunized, antibody was produced at a slower rate than in those calves possessing little or no maternally-derived antibody.

The development of an active immunity to rinderpest by these calves possessing maternally-derived antibody was not necessarily associated with a clinical reaction. When passively immune calves failed to produce antibodies following caprinized rinderpest virus inoculation, sensitization of the antibody-forming mechanism did not occur as was demonstrated by failure to show an anamnestic response following later exposure to rinderpest antigen.

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